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Brief Communication

Increases in duration of first uninterrupted sleep period are associated with improvements in PSQI-measured sleep quality

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ABSTRACT

Objective: Urology clinical trials assessing bladder function have relied on the self-reported duration of the first uninterrupted sleep period (FUSP) as a proxy outcome for sleep, but the relationship between this measure and more conventional self-reported measures of sleep is unknown. In this study, we examined the association between changes in FUSP and a widely used self-reported measure of sleep, the Pittsburgh Sleep Quality Index (PSQI).
Methods: We conducted post hoc (secondary) analyses of unpublished data from a previously published randomized clinical trial (NCT00477490) of desmopressin (a medication used to treat nocturia) and examined relationships between baseline and 4-week change in FUSP and PSQI global and subscale scores for participants ($N = 580$ to $N = 606$) having complete data.
Results: Data indicated strong associations between change in PSQI global score and FUSP change in six of seven subscale scores. A reduction of 1.8 points in the PSQI global score was associated with a 72-min lengthening of FUSP.
Conclusions: Results suggest that FUSP is a potentially valuable metric that correlates with changes in perceived sleep duration, depth, quality for the entire night, efficiency, latency, and daytime function. An increase in FUSP was related to improvement in nearly all PSQI subscales. The validity of this measure in the general population remains to be determined.

1. Introduction

The first uninterrupted sleep period (FUSP) has been used as a self-reported outcome in studies of various urological conditions including benign prostatic obstruction (BPO) [1], overactive bladder (OAB) [2], and nocturia [3]. How this outcome relates to other, better recognized measures of sleep quality remain unclear. In this post hoc analysis, we compared data on FUSP from a phase III trial of a nocturia medication [4], which also included previously unpublished data on the Pittsburgh Sleep Quality Index (PSQI) [5], to determine how closely changes in FUSP related to changes in various aspects of self-reported sleep on PSQI.

2. Methods

Data were derived from a registered phase III trial (http://www.clinicaltrials.gov: NCT00477490) of the orally dispersible tablet (ODT) formulation of desmopressin in nocturia patients who reported two or more voids/night. This was an institutional review board-approved, 4-week, randomized, placebo-controlled study of four doses of desmopressin ODT (10, 25, 50, and 100 μg), and details of the inclusion criteria are described in the primary manuscript presenting data from this trial [4]. Sedative/hypnotic medications and OAB medications were permitted as long as the patient had been on a stable dose for three months prior to screening. Initiation of these medications or any change in dose or discontinuation of therapy for subjects who entered the trial on these medications constituted a protocol violation and data were excluded from the current analyses. Patients with renal disease, male patients with BPO or prior history of urological malignancies, and female patients with a history of pelvic prolapse were excluded.

FUSP was defined as the elapsed time in minutes from turning off the light intending to go to bed to the time of the first nocturnal void, or until the time of final awakening (if no void occurred), minus the time in minutes it took the subject to fall asleep. FUSP was recorded in a 3-day voiding and sleep diary completed at baseline, and immediately prior to the week 4 visit at the end of the double-blind period. The average FUSP over the 3-day voiding and sleep diary was summarized for the baseline and 4-week time periods. Similarly, the PSQI (utilizing the customary 30-day time

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Table 1
Associations between FUSP increase and improvement in PSQI component scales.[a]

PSQI Scale Component	*n*	Raw score parameter estimate[b] (1-h increase in FUSP)	SE	*Z*-score parameter estimate[c] (1-h increase in FUSP)	SE	*p* value
Global	580	–0.5367	0.0588	–0.1791	0.0196	<0.0001
Sleep quality	605	–0.1165	0.0133	–0.1634	0.0187	<0.0001
Sleep latency	582	–0.0828	0.0161	–0.1106	0.0214	<0.0001
Sleep duration	604	–0.0787	0.0144	–0.1030	0.0189	<0.0001
Sleep efficiency	604	–0.1253	0.0200	–0.1245	0.0198	<0.0001
Sleep disturbances	606	–0.0443	0.0130	0.0665	0.0195	0.0007
Sleep medication	606	–0.0165	0.0178	–0.0198	0.0213	0.3545
Daytime dysfunction	606	–0.0783	0.0150	–0.0970	0.0186	<0.0001

[a] ANCOVAs on respective PSQI scale component changes controlling for respective baseline PSQI score, age, baseline FUSP, and change in FUSP as covariate; parameter estimates shown only for 1-h change in FUSP for each PSQI scale; higher PSQI score indicates poorer sleep; *n* is sample size at Month 1.
[b] PSQI raw global scale range: 0–21; subscore scale range: 0–3.
[c] Standardized *z*-score based on the population mean and SD.

frame) was completed at baseline and at the end of the 4-week double-blind period.

A post hoc analysis of a subgroup of patients who completed both the diaries and PSQI at baseline and at the week 4 visit was performed pooling all treatment groups. The change from baseline in PSQI components and FUSP were analyzed using analyses of covariance (ANCOVA) adjusting for age and baseline value. The relationship between the change in FUSP and change in PSQI was analyzed using an ANCOVA model of the change from baseline on respective PSQI scale components, controlling for baseline PSQI score, age, and baseline FUSP, with change in FUSP as a covariate.

3. Results

The intent-to-treat (ITT) population comprised 757 patients (416 men and 341 women; mean age = 62.0; standard deviation, SD = 13.1; range 20–89) who awakened an average of 3.3 times per night to void. A subgroup of patients ($n = 580$ to $n = 606$), who provided data both on FUSP and on the PSQI global or subscale scores both at baseline and on week 4, were included in the current analyses. The subgroup had similar demographics (gender and age) and baseline values for FUSP and PSQI with the entire ITT population.

At baseline, the mean FUSP was 116.0 (SD = 62.8) min, and the mean baseline global PSQI was 8.2 (3.8). During the 4-week study, patients experienced an average increase of 72.4 min (95% confidence interval (CI) 64.3, 80.5; $p < 0.0001$) in FUSP, after adjusting for baseline value and age. The adjusted mean reduction from baseline to week 4 in the PSQI global score was –1.8 (95% CI –2.0, –1.6; $p < 0.0001$). As shown in Table 1, a 1-h increase in FUSP was associated with highly significant changes in the PSQI global score and six out of seven component scores. The direction of those changes uniformly indicated improved sleep associated with increased FUSP.

4. Discussion

This is the first study to investigate the relationship between dynamic changes in FUSP, often reported as a proxy for sleep quality in trials of nocturia, and a widely used index of self-reported sleep encompassing the whole night, the PSQI. The results demonstrated that increasing durations of the period of sleep prior to the first nocturnal void were significantly associated with improvements in the global PSQI score, as well as component scores reflecting sleep quality, latency, duration, efficiency, disturbances, and daytime dysfunction. The magnitude of the effect here with the global score (i.e., a change in 1.8 points) is roughly comparable to the magnitude of change seen in various clinical trials focused on exercise interventions for insomnia (2.1 points) [6], improvements in sleep when treating gastroesophageal reflux with esomeprazole (2.9 points) [7], effects of tai chi on sleep (2.1 points) [8], behavioral interventions for improved sleep in osteoarthritis patients (1.5 points) [9], generalized anxiety disorders (1.9 points) [10] or decreased hypnotic drug use (2.8 points) [11], and reduction of sleep symptoms associated with menopause with escitalopram (2.6 points) [12] or gabapentin (2.6 points) [13] in women with nocturnal menopausal symptoms. The fact that, in our data, the 4-week change in global PSQI remained above 5 (the commonly accepted threshold for defining poor sleep) [14] suggests that the study population continued to have some problems with sleep, even after their nocturia was successfully treated. Similar results were noted in many of the aforementioned trials as well [6,8–13]. The global PSQI score, relative to the subscale scores, is most typically used in clinical trials, though some intervention studies also report change in subscales (e.g., 6, 8, 10, and 13).

Nocturia is among the most frequently cited reasons for disturbed sleep in older adults [15–18] in the general population. Interestingly, nocturia has only been recognized by urologists as a condition in its own right for about a decade, distinct from conditions more commonly thought to be associated with its occurrence, such as bladder outlet obstruction in men, low estrogen in women, and detrusor overactivity or bladder storage capacity, in both men and women [19]. Our data suggest that FUSP may serve as a useful measure, not only in trials of bladder medications but also for sedative/hypnotic trials and for behavioral sleep interventions as well. For example, recent work has shown that obtaining information about nocturia predicted the relative success or failure of a behavioral intervention for poor sleep [20]. Ironically, most sleep diaries simply do not ask about nocturia as a component of nighttime awakenings resulting in bathroom trips [21]. Data on FUSP could also be easily collected with traditional sleep diaries, although these are not customarily analyzed. The current data suggest that FUSP may be a good measure to include in both interventional and descriptive studies of insomnia. Improvements in FUSP in nocturia treatment also have been associated with improvements in various quality-of-life measures [22,23].

Limitations of the current analyses include the fact that the strong relationships between FUSP and PSQI were detected in a clinical population with nocturia that may not translate directly to normal, healthy populations; further research is needed to confirm the correlation between FUSP and PSQI generally. Additionally, the abbreviated diary used in this study to collect data on FUSP did not collect data on other aspects of sleep such as whether the nocturnal voiding trip was perceived as a cause or consequence of the awakening. Finally, the trial generating the data in this report employed randomization with subjects stratified on a 1:1 basis over and under age 65, raising the possibility that, despite controlling for age, associations between FUSP and sleep quality may have been carried

by the relative high proportion of older participants in this study. Nonetheless, because nocturia has been shown to be related to poor sleep, lower quality of life, and depression across a wide age range in adults [16,24–26], the robustness of this simple self-reported marker suggests consideration of its potential use in other populations as well.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.05.010.

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